

**REMARK**

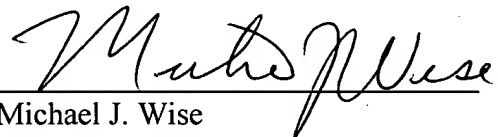
These amendments are to correct errors that are typographical in nature, and therefore introduce no new matter into the disclosure of this application.

No fee is believed to be due with this amendment. However, if Applicants are in error, the Commissioner is authorized to charge required fees to Lyon & Lyon's Deposit Account No. 12-2475.

Respectfully submitted,  
LYON & LYON LLP

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By: \_\_\_\_\_

  
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**MARKED-UP VERSION OF AMENDMENT**

In the Claims:

113. (Twice Amended) The method of claim 100, wherein the mutated steroid hormone receptor ligand binding domain binds a compound selected from the group consisting of 5-alpha-pregnane-3,20-dione[3,2-dione]; 11β-(4-dimethylaminophenyl)-17β-hydroxy-17α-propinyl-4,9-estradiene-3-one; 11β-(4-dimethylaminophenyl)-17α-hydroxy-17β-(3-hydroxypropyl)-13α-methyl-4,9-gonadiene-3-one; 11β-(4-acetylphenyl)-17β-hydroxy-17α-(1-propinyl)-4,9-estradiene-3-one; 11β-(4-dimethylaminophenyl)-17β-hydroxy-17α-(3-hydroxy-1(Z)-propenyl-estra-4,9-diene-3-one; (7β,11β,17β)-11-(4-dimethylaminophenyl)-7-methyl-4',5'-dihydrospiro(ester-4,9-diene-17,2'(3'H)-furan)-3-one; (11β,14β,17α)-4',5'-dihydro-11-(4-dimethylaminophenyl)-(spiroestra-4,9-diene-17,2'(3'H)-furan)-3-one.

In the Specification:

On page 7, lines 1-10, please delete the paragraph and replace it with the following:

Specific examples of compounds which bind the ligand binding domain include 5-alpha-pregnane-3,20-dione[3,2-dione]; 11β-(4-dimethylaminophenyl)-17β-hydroxy-17α-propinyl-4,9-estradiene-3-one; 11β-(4-dimethylaminophenyl)-17α-hydroxy-17β-(3-hydroxypropyl)-13α-methyl-4,9-gonadiene-3-one; 11β-(4-acetylphenyl)-17β-hydroxy-17α-(1-propinyl)-4,9-estradiene-3-one; 11β-(4-dimethylaminophenyl)-17β-hydroxy-17α-(3-hydroxy-1(Z)-propenyl-estra-4,9-diene-3-one; (7β,11β,17β)-11-(4-dimethylaminophenyl)-7-methyl-4',5'-dihydrospiro[[[(ester-4,9-diene-17,2'(3'H)-furan)]]]-3-one; (11β,14β,17α)-4',5'-dihydro-11-(4-dimethylaminophenyl)- [[[(spiroestra-4,9-diene-17,2'(3'H)-furan)]]]-3-one.

On page 10, lines 11-22, please delete the paragraph and replace it with the following:

Examples of non-natural ligands, anti-hormones and non-native ligands include the following: 11 $\beta$ -(4-dimethylaminophenyl)-17 $\beta$ -hydroxy-17 $\alpha$ -propinyl-4,9-estradiene-3-one (RU38486 or Mifepristone[Mifepestone]); 11 $\beta$ -(4-dimethylaminophenyl)-17 $\alpha$ -hydroxy-17 $\beta$ -(3-hydroxypropyl)-13 $\alpha$ -methyl-4,9-gonadiene-3-one (ZK98299 or Onapristone); 11 $\beta$ -(4-acetylphenyl)-17 $\beta$ -hydroxy-17 $\alpha$ -(1-propinyl)-4,9-estradiene-3-one (ZK112993); 11 $\beta$ -(4-dimethylaminophenyl)-17 $\beta$ -hydroxy-17 $\alpha$ -(3-hydroxy-1(Z)-propenyl-estra-4,9-diene-3-one (ZK98734); (7 $\beta$ ,11 $\beta$ ,17 $\beta$ )-11-(4-dimethylaminophenyl)-7-methyl-4',5'-dihydrospiro[[[ester-4,9-diene-17,2'(3'H)-furan]]]-3-one (Org31806); (11 $\beta$ ,14 $\beta$ ,17 $\alpha$ )-4',5'-dihydro-11-(4-dimethylaminophenyl)-[[[spiroestra-4,9-diene-17,2'(3'H)-furan]]]-3-one (Org31376); 5-alpha-pregnane-3,20-dione[3,2-dione].

Starting on page 19, line 26 and ending on page 20, line 5, please delete the paragraph and replace it with the following:

Side chains are usually tolerated at certain positions on ligands of the receptor superfamily. For example, the 7-alpha position of certain ligands, such as estradiol and progesterone, can be attached to sidechains and the ligands will still bind to receptors. Suitable sidechains can be used to either increase or restrict solubility, membrane transfer or target organ accessibility. Thus, even specific ligands can be made to show tissue preference. For example, the synthetic steroid R5020 (17 $\alpha$ ,21-dimethyl-19-Norpregna[Norpregn]-4,9-diene-3,20-dione) does not enter tissue culture cells at low temperatures at which progesterone enters freely. One skilled in the art readily recognizes that other modifications can be made to ligands to tailor their use as up- or down-regulating agents in the present invention.